



Patent Application  
Docket No. SPO-113

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : Kenji Kadomatsu, Mitsuru Horiba, Takashi Muramatsu, Shinya Ikematsu,  
Sadatoshi Sakuma

Docket No. : SPO-113

For : Pharmaceutical Compositions For The Prevention And Treatment Of  
Atherosclerosis And Restenosis After PTCA

Box PCT  
Assistant Commissioner for Patents  
Washington, D.C. 20231

**CERTIFICATE OF MAILING BY EXPRESS MAIL (37 CFR §1.10)**

Express Mail No.: **EK507535295US**, of Deposit: February 22, 2001

I hereby certify that the attached Transmittal Letter to the United States Designated/Elected Office (DO/EO/US); Preliminary Amendment; Declaration (37 CFR §1.63) and Power of Attorney; Submission of Sequence Listing Under 37 CFR 1.821 - 1.825; Replacement Sequence Listing on paper pages 1-8; and computer readable format containing the same information on disk with copies as required for authorization for use of Deposit Account No. 19-0065, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and are addressed to: Box PCT, Assistant Commissioner for Patents, Washington, D.C. 20231.

Sangreal Smith  
Name of person mailing paper

  
Signature

JCT Rec'd PCT/PTO 13 MAR 2002  
PCT



I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:  
Commissioner of Patents and Trademarks,  
Washington, D.C. 20231 on March 5, 2002.

David Saliwanchik  
David R. Saliwanchik, Patent Attorney

Patent Application  
Docket No. SPO 13  
Serial No. 09/763,586

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CFR

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Kenji Kadomatsu, Mitsuru Horiba, Takashi Muramatsu, shinya Ikematsu, Sadatoshi Sakuma  
Serial No. : 09/763,586  
Conf. No. : 7871  
Filed : February 22, 2001  
For : Pharmaceutical Compositions For the Prevention and Treatment of Atherosclerosis and Restenosis After PTCA

Office of Initial Patent Examination  
Customer Service Center  
Commissioner of Patents and Trademarks  
Washington, D.C. 20231

REQUEST FOR CORRECTION OF FILING RECEIPT

Sir:

The applicants respectfully request the correction of errors in the official Filing Receipt for the above-identified patent application. Clerical errors have occurred in the title of the application and in the residence section of the applicants. The correction needed is as follows:

Title

Preventives/remedies for arteriosclerosis and post-ptca reangiostenosis

should read

**Pharmaceutical Compositions For the Prevention and Treatment of Atherosclerosis and  
Restenosis After PTCA**

**Applicant(s)**

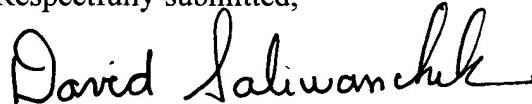
Kenji Kadomatsu, Nagoya-shi, JAPAN;  
Mitsuru Horiba, Nagoya-shi, JAPAN;  
Takashi Muramatsu, Nagoya-shi, JAPAN;  
Shinya Ikematsu, Odawara-shi, JAPAN;  
Sadatoshi Sakuma, Odawara-shi, JAPAN;

**Should read:**

Kenji Kadomatsu, Aichi, JAPAN;  
Mitsuru Horiba, Aichi, JAPAN;  
Takashi Muramatsu, Aichi, JAPAN;  
Shinya Ikematsu, Kanagawa, JAPAN;  
Sadatoshi Sakuma, Kanagawa, JAPAN;

A copy of the erroneous Official Filing Receipt accompanies this Request. Also, attached is a copy of page 1 of the Transmittal Letter Form PTO-1390 page 1 of the subject specification and a copy of the Declaration and Power of Attorney. Correction of the above is respectfully requested.

Respectfully submitted,



David R. Saliwanchik  
Patent Attorney  
Registration No. 31,794  
Phone No.: 352-375-8100  
Address : 2421 N.W. 41st Street, Suite A-1  
Gainesville, FL 32606-6669

DRS/la

Enclosures: Copy of erroneous Filing Receipt;  
Page 1 of Form PTO-1390;  
Page 1 of subject application; and  
Copy of Declaration and Power of Attorney form.

O I P E  
MAR 13 2002  
U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

**TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371**

ATTORNEY'S DOCKET NUMBER

SPO-113

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

INTERNATIONAL APPLICATION NO.  
PCT/JP99/04550INTERNATIONAL FILING DATE  
24 August 1999PRIORITY DATE CLAIMED  
24 August 1998TITLE OF INVENTION Pharmaceutical Compositions For The Prevention And Treatment Of  
Atherosclerosis And Restenosis After PTCAAPPLICANT(S) FOR DO/EO/US Kenji Kadomatsu, Mitsuru Horiba, Takashi Muramatsu,  
Shinya Ikematsu, Sadatoshi Sakuma

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1.  This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2.  This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3.  This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)).
4.  The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5.  A copy of the International Application as filed (35 U.S.C. 371(c)(2))
  - a.  is attached hereto (required only if not communicated by the International Bureau).
  - b.  has been communicated by the International Bureau.
  - c.  is not required, as the application was filed in the United States Receiving Office (RO/US).
6.  An English language translation of the International Application as filed (35 U.S.C. 371(c)(1)).
7.  Amendments to the claims of the International Application under PCT Article 19(35 U.S.C. 371(c)(3))
  - a.  are attached hereto (required only if not communicated by the International Bureau).
  - b.  have been communicated by the International Bureau.
  - c.  have not been made; however, the time limit for making such amendments has NOT expired.
  - d.  have not been made and will not be made.
8.  An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9.  An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (unsigned)
10.  An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 16 below concern document(s) or information included:

11.  An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12.  An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13.  A FIRST preliminary amendment.
- A SECOND or SUBSEQUENT preliminary amendment.
14.  A substitute specification.
15.  A change of power of attorney and/or address letter.
16.  Other items or information: Submission of Sequence Listing Under 37 CFR 1.821-1.825



- 1 -

## DESCRIPTION

### PHARMACEUTICAL COMPOSITIONS FOR THE PREVENTION AND TREATMENT OF ATHEROSCLEROSIS AND RESTENOSIS AFTER PTCA

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#### Technical field

The present invention relates to pharmaceutical compositions for the prevention and treatment of disorders attributed to intimal thickening, more specifically to pharmaceutical compositions for the 10 prevention and treatment of these diseases, comprising MK or its inhibitor as an effective ingredient.

#### Background Art

Incidence of ischemic cardiac diseases caused by arteriosclerosis, 15 especially, coronary arteriosclerosis, such as angina pectoris, and myocardial infarction are recently on the increase. Pathological tissue images of arteriosclerosis mainly show local intimal thickening and diminished elasticity. As a result, circulation is disturbed, and nutrients and oxygen are insufficiently supplied to myocardial tissues, 20 leading to the above-mentioned conditions.

Many important findings have been made regarding the pathogenesis of intimal thickening. A typical example is that the thickened intima primarily constitutes of smooth muscle cells that migrated from tunica media (Parker, F., Amer. J. Pathol., 1960, 36, 19-53; and Webster, W. 25 S., S. P. Bishop & J. C. Geer, Amer. J. Pathol., 1974, 76, 245-264). Moreover, the hypothesis that arteriosclerosis develops as a result of the injury-repairing reaction (Ross, R., N. Engl. J. Med., 1986, 314, 488-500) is the base of understanding on arteriosclerosis even now.

Percutaneous transluminal coronary angioplasty (PTCA), a 30 treatment in which a blood vessel constricted by such an intimal thickening is inflated by a balloon and physically expanded, is a common treatment at present. PTCA surgery has proved to be remarkably effective with a 90% or higher recovery rate. However, restenosis occurs with a frequency of 30 to 60% at the same site within 6 months 35 or less following PTCA. It is pathologically recognized that restenosis is the result of an excessive repairing mechanism, the excessive